Amendment to the Specification:

Please amend the Specification as follows:

On page 14, beginning on line 8, please substitute the following paragraph:

Suitable components for use in such vaccines are already commercially available and details may be obtained from the World Health Organisation. For example the IPV component may be the Salk inactivated polio vaccine. The Hepatitis B surface antigen may comprise the 'S' antigen as in ~~Engerix-B™~~ ENGERIX-B® (SmithKline Beecham Biologicals).

On page 20, beginning on line 15, please substitute the following paragraph:

Three types of mixing steps were followed to demonstrate the efficacy of PLG in reducing the physical interaction between PRP-T and $Al(OH)_3$, including mixing the commercially available ~~Infanrix Penta™~~ INFANRIX PENTA™ (DTPaHepBIPV) vaccine with Hib-PLG vaccine:

- Step 1: pre-saturation whereby PLG was first adsorbed on $Al(OH)_3$, then PRP-T was added.
- Step 2: competition whereby PLG was put in competition with PRP-T for adsorption on $Al(OH)_3$
- ~~Infanrix Penta™~~ INFANRIX PENTA™/Hib-PLG: whereby PLG and PRP-T were co-lyophilized and then put in competition for adsorption in ~~Infanrix-PeNTa™~~ INFANRIX PENTA™ vaccine, containing 500µg $Al(OH)_3$

On page 20, beginning on line 30, please substitute the following paragraph:

The 200µM PLG (Mw 2,200) content was selected for clinical formulation as:

- no flocculation was observed,
- close to 80% PRP-T was non-adsorbed (according to the Dionex test)
- PLG is fully adsorbed
- all major components of ~~Infanrix~~ INFANRIX® (DT, TT, PT, FHA, PRN [or 69K], IPV and HB surface antigen) were not affected.
- Both lactose and sucrose were found to be efficient cryoprotectors.

On page 21, beginning on line 7, please substitute the following paragraph:

Figure 2 shows the competition between PRP-T and PLG (85 residues). 100µM PLG Mw 10,900 are able to limit adsorption of 10µg Hib on 50 (to mimic hypothetical free $Al(OH)_3$ in ~~Infanrix PeNTa~~ INFANRIX PENTA™) as

well as on 500µg $Al(OH)_3$ (= full $Al(OH)_3$ dose in ~~Infanrix PeNTa~~ INFANRIX PENTA ™).

On page 21, beginning on line 12, please substitute the following paragraph:

In addition, 500µm PLG Mw 2,178 (17 residues) are able to limit adsorption of 10µg Hib on $Al(OH)_3$ after reconstitution of [Hib-PLG] cake with ~~Infanrix PeNTa~~ INFANRIX PENTA ™ (1h contact, then centrifugation 6min 6500g and dosage of Hib in supernatant by ELISA PRR'P-TT or Dionex dosage) , as can 75µM PLG Mw 10,900 (85 residues).

On page 21, beginning on line 17, please substitute the following paragraph:

PLG Mw 2,178 (17 residues) is able to limit adsorption of 5µg Hib (PRP-T) on $Al(OH)_3$ after reconstitution of [Hib-PLG] cake with ~~Infanrix PeNTa~~ INFANRIX PENTA ™ (1h contact, then centrifugation 6min 6500g and dosage of Hib in supernatant by ELISA PRR'P-TT or Dionex dosage) - 175 and 200µM were optimal concentrations in that there is an absence of flocculation and ~~Infanrix~~ INFANRIX® antigen adsorption is retained.

On page 21, beginning on line 23, please substitute the following paragraph:

PLG Mw 10,800 (85 residues) is able to limit adsorption of 5µg Hib (amount of PRP in PRP-T) on $Al(OH)_3$ after reconstitution of [Hib-PLG] cake with ~~Infanrix PeNTa~~ INFANRIX PENTA ™ (1h contact, then centrifugation 6min 6500g and dosage of Hib in supernatant by ELISA PRR'P-TT or Dionex dosage) - 30 and 35µM were optimal concentrations in that there is an absence of flocculation and ~~Infanrix~~ INFANRIX® antigen adsorption is retained.

On page 21, beginning on line 31, please substitute the following paragraph:

Hib-PLG experimental formulations were evaluated in a rabbit model of immunogenicity and a baby rat model allowing evaluation of the Hib (PRP-T conjugate) immune interference induced by combination of ~~Infanrix Penta~~ INFANRIX PENTA ™ and Hib vaccines. Moreover, impact of Hib-PLG on the efficacy of ~~Infanrix Penta~~ INFANRIX PENTA ™ was evaluated in a *B. pertussis* lung colonization murine model.

On page 23, beginning on line 7, please substitute the following paragraph:

As a control of interference in the baby rat model, Hib combined with ~~Infanrix-Penta~~ INFANRIX PENTA™ (10 µg PRP) was administered as well as Hib (10µg) co-administered with ~~Infanrix Penta~~. INFANRIX PENTA™ Hib (5 µg) formulated alone or containing various amounts of PLG were evaluated after reconstitution with ~~Infanrix Penta~~ INFANRIX PENTA™.

On page 23, beginning on line 11, please substitute the following paragraph:

See below for details of vaccines administered by group

Group	Vaccine
1	Hib (10µg) + ~~Infanrix Penta~~ INFANRIX PENTA™
2	Hib (10µg) reconstituted with ~~Infanrix Penta~~ INFANRIX PENTA™
3	Hib (5µg) PLG HMW (10900) 30µM reconstituted with ~~Infanrix Penta~~ INFANRIX PENTA™
4	Hib (5µg) PLG HMW (10900) 75µM reconstituted with ~~Infanrix Penta~~ INFANRIX PENTA™
5	Hib (5µg) PLG LMW (2200) 175µM reconstituted with ~~Infanrix Penta~~ INFANRIX PENTA™
6	Hib (5µg) PLG LMW (2200) 500µM reconstituted with ~~Infanrix Penta~~ INFANRIX PENTA™
7	Hib (5µg) reconstituted with ~~Infanrix Penta~~ INFANRIX PENTA™

On page 23, beginning on line 16, please substitute the following paragraph:

When Hib is administered with ~~Infanrix Penta~~ INFANRIX PENTA™ immune interference was observed as compared with Hib co-administered separately with ~~Infanrix Penta~~ INFANRIX PENTA™.

On page 24, beginning on line 10, please substitute the following paragraph:

5 μg (saccharide) of PRP-T (Hib) was combined with different amounts of PLG (Sigma) of Mw 2,600 to realise either 0, 175 or 200 μM final concentration in the reconstituted vaccine. The samples were lyophilised in the presence of sucrose. The samples were then reconstituted with ~~Infanrix PeNTa~~ INFANRIX PENTA ™ and after 1 hour the recovery of unadsorbed antigen in the supernatant (s/n) was measured. The results were as below:

On page 25, beginning on line 12, please substitute the following paragraph:

The reconstitution of DTPaHepB IPV with Hib conjugate induces flocculation of the aluminium contained in DTPaHepB IPV (see Figure 5). These may be observed visually and by optical microscopy, and may be measured by size and sedimentation analysis. Figure 7 shows an optical microscope picture of ~~Infanrix peNTa~~ INFANRIX PENTA ™ (DTPaHepBIPV). Figure 8 shows the sample flocculating when 5μg saccharide of PRP-TT is added to the sample. Figure 9 shows that no flocculation occurs in the presence of 200 μM PLG Mw 2,200 (Sigma).

On page 25, beginning on line 24, please substitute the following paragraph:

The DTPaHepB IPV (~~Infanrix~~ INFANRIX®) tested had 500 μg $Al(OH)_3$, 200 μg $AlPO_4$ per human dose. The DTPwHepB (~~Tritanrix~~TRITANRIX ™) tested had 260 μg $Al(OH)_3$, 370 μg $AlPO_4$ per human dose. PRP-TT (Hib) was unadjuvanted, as were the MenA-TT and MenC-TT capsular polysaccharide conjugates. 5 g saccharide of the conjugates per dose were used in all experiments.

On page 30, beginning on line 18, please substitute the following paragraph:

- The immune response to PRP after vaccination with DTPa-HBV-IPV/Hib PLG was similar to that to ~~Hiberix~~ HIBERIX® (Hib vaccine) and statistically higher than the response to ~~Infanrix hexa~~ INFANRIX HEXA ™(DTPa-HBV-IPV/Hib vaccine) ($p<0.05$), both in terms of GMCs and of seroprotection rates (Table 1).

On page 30, beginning on line 25, please substitute the following table:

Table 1: response to the PRP antigen in the three study groups ((ATP cohort for immunogenicity)

Group	Timing	N	≥0.15 µg/ml				≥ 1 µg/ml				GMC (µg/ml)		
			n	%	95% CI		n	%	95% CI		Value	95% CI	
					LL	UL			LL	UL		LL	UL
DTPa-HBV-IPV/HibPLG	PRE	48	17	35.4	22.2	50.5	1	2.1	0.1	11.1	0.137	0.106	0.179
	PIII	47	47	100.0	92.5	100.0	36	76.6	62.0	87.7	3.375	2.314	4.924
DTPa-HBV-IPV/Hib	PRE	49	18	36.7	23.4	51.7	6	12.2	4.6	24.8	0.177	0.122	0.255
	PIII	49	42	85.7	72.8	94.1	29	59.2	44.2	73.0	1.164	0.711	1.904
DTPa-HBV-IPV +	PRE	50	17	34.0	21.2	48.8	4	8.0	2.2	19.2	0.153	0.112	0.209
~~Hiberix~~HIBERIX®	PIII	50	48	96.0	86.3	99.5	36	72.0	57.5	83.8	3.014	1.846	4.920

N: number of subjects with available results
%: percentage of subjects with anti-PRP concentration above the specified cut-off
95% CI; LL, UL: 95% confidence interval; lower and upper limit

Table 2: Percentage of subjects seroprotected and vaccine response to pertussis antigens after primart vaccination (ATP cohort for immunogenicity)

	DTPa-HBV-IPV/HibPLG				DTPa-HBV-IPV/Hib				DTPa-HBV-IPV + ~~Hiberix~~HIBERIX®			
	N	%	95%CI		N	%	95%CI		N	%	95%CI	
			LL	UL			LL	UL			LL	UL
Seroprotection												
Anti-D (≥ 0.1 IU/ml)	48	97.9	88.9	99.9	49	100	92.7	100	50	100	92.9	100
Anti-T (≥ 0.1 IU/ml)	47	100	92.5	100	49	100	92.7	100	50	100	92.9	100
Anti-HBs (≥ 10 mIU/ml)	47	100	92.5	100	49	100	92.7	100	50	98.0	89.4	99.9
Anti-polio 1 (≥ 8)	33	100	89.4	100	41	100	91.4	100	41	100	91.4	100
Anti-polio 2 (≥ 8)	34	100	89.7	100	39	97.4	86.5	99.9	36	100	90.3	100
Anti-polio 3 (≥ 8)	32	100	89.1	100	34	100	89.7	100	33	100	89.4	100
Vaccine response												
Anti-PT	48	100	92.6	100	48	97.9	88.9	99.9	48	93.8	82.8	98.7
Anti-FHA	48	89.6	77.3	96.5	49	93.9	83.1	98.7	50	90.0	78.2	96.7
Anti-PRN	48	91.7	80	97.7	49	95.9	86	99.5	50	90.0	78.2	96.7

N: number of subjects with available results
%: percentage of subjects seroprotected or with vaccine response
95% CI; LL, UL: 95% confidence interval; lower and upper limit

On page 31, beginning on line 7, please substitute the following table:

Table 3: Safety results for the ATP safety cohort.

		DTPa-HBV-IPV/HibPLG (N=49)				DTPa-HBV-IPV/Hib (N=50)				DTPa-HBV-IPV + ~~Hiberix~~HIBERIX® (N=51)			
	Intensity	**n**	**%**	**95% CI**		**n**	**%**	**95% CI**		**n**	**%**	**95% CI**	
Solicited local symptoms													
Pain	Any	19	38.8	25.2	53.8	17	34.0	21.2	48.8	20	39.2	25.8	53.9
	Grade "3"	0	0.0	0.0	7.3	1	2.0	0.1	10.6	2	3.9	0.5	13.5
Redness	Any	27	55.1	40.2	69.3	26	52.0	37.4	66.3	23	45.1	31.1	59.7
	> 20 mm	1	2.0	0.1	10.9	4	8.0	2.2	19.2	4	7.8	2.2	18.9
Swelling	Any	20	40.8	27.0	55.8	17	34.0	21.2	48.8	20	39.2	25.8	53.9
	> 20 mm	6	12.2	4.6	24.8	5	10.0	3.3	21.8	11	21.6	11.3	35.3
Solicited general symptoms:													
Drowsiness	Any	22	44.9	30.7	59.8	26	52.0	37.4	66.3	26	51.0	36.6	65.2
	Grade "3"	1	2.0	0.1	10.9	1	2.0	0.1	10.6	0	0.0	0.0	7.0
	Related	22	44.9	30.7	59.8	24	48.0	33.7	62.6	24	47.1	32.9	61.5
Irritability	Any	29	59.2	44.2	73.0	30	60.0	45.2	73.6	30	58.8	44.2	72.4
	Grade "3"	4	8.2	2.3	19.6	1	2.0	0.1	10.6	3	5.9	1.2	16.2
	Related	28	57.1	42.2	71.2	28	56.0	41.3	70.0	29	56.9	42.2	70.7
Loss of appetite	Any	17	34.7	21.7	49.6	16	32.0	19.5	46.7	14	27.5	15.9	41.7
	Grade "3"	0	0.0	0.0	7.3	0	0.0	0.0	7.1	0	0.0	0.0	7.0
	Related	17	34.7	21.7	49.6	13	26.0	14.6	40.3	12	23.5	12.8	37.5
Fever	≥ 38 °C	7	14.3	5.9	27.2	8	16.0	7.2	29.1	8	15.7	7.0	28.6
	>38.5 °C	2	10.5	3.4	22.2	8	16.0	7.2	29.1	7	13.7	5.7	26.3
	>39 °C	0	0.0	0.0	7.3	0	0.0	0.0	7.1	2	3.9	0.5	13.5
	> 39.5 °C	0	0.0	0.0	7.3	0	0.0	0.0	7.1	0	0.0	0.0	7.0
	Related	5	10.2	3.4	22.2	8	16.0	7.2	29.1	7	13.7	5.7	26.3

On page 32, beginning on line 2, please substitute the following paragraph:

• The Hib response after vaccination with DTPa-HBV-IPV/HibPLG was significantly higher as compared to DTPa-HBV-IPV/Hib and was not different from that to the standalone Hib conjugate vaccine ~~Hiberix~~HIBERIX®. There was thus no observed Hib immune interference problem with the new formulation.